region. While mutations conferring resistance to azithromycin are well established, this is not the case for fluoroquinolones. We aimed to define mutations associated with fluoroquinolone failure to inform next generation resistance assays.

Methods Samples from patients undergoing resistance-guided therapy with either moxifloxacin (Apr-2017–Jun-2018, 202 cases: 21 moxifloxacin failures) or sitafloxacin (Jun-2016–May-2017, 125 cases:12 sitafloxacin failures) were sequenced for key regions of parC and gyrA genes. Chi-square or Fisher’s exact tests were used to examine prevalence of each mutation and treatment outcome.

Results In an interim analysis the most common parC mutations were G248T (amino acid change S83I; 16%), G259A (D87N; 4%), G248A (S83N; 1%) and mutations effecting S83R (1%). G248T (S83I) mutation was more common among patients that failed moxifloxacin [15/21 failures (71%) vs 11/181 cures (6%), p<0.001] and sitafloxacin [6/12 failures (50%) vs 19/113 cures (17%), p=0.0063]. Notably, sitafloxacin cured a higher proportion of infections carrying the S83I mutation than moxifloxacin (76% vs 42%; p=0.015). ParC D87N was not associated with failure of moxifloxacin [1/21 failures (5%) vs 11/181 cures (6%)]. The most common gyrA mutations were G285A (M95I; 5%) and G295T (D99Y; 1%). An infection with an S83I mutation was more likely to fail treatment when combined with a gyrA mutation (M95I or D99N) (4/6 sitafloxacin failures with parC. S83I also had gyrA mutation, compared to 1/16 cures; p=0.0093), suggesting an additive effect.

Conclusion This study provides compelling evidence that parC G248T (S83I) mutations contribute to failure of moxifloxacin and sitafloxacin used for macrolide-resistant M. genitalium. These data will inform the development of quinolone resistance assays needed to ensure optimal selection of antimicrobials in M. genitalium.

Disclosure No significant relationships.

Abstracts

004.5 POINT-OF-CARE MAGNETOFUIDIC ASSAY CARTRIDGE FOR NEISSERIA GONORROEAE DETECTION AND ANTIMICROBIAL RESISTANCE DETERMINATION

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Background The rise of antimicrobial resistant (AMR) Neisseria gonorrhoeae (NG) has prompted worldwide concern over the looming possibility of untreatable gonococcal infections. A reduction of antimicrobial use by transitioning from generalized prescriptions to targeted pathogen-specific treatments would aid in treatment efficacy and reduce the risk of AMR NG development. However, actual implementation of such targeted treatments has been limited by the lack of rapid diagnostic tools that can provide antimicrobial susceptibility results at the point-of-care (POC).

Methods To address the need for a rapid NG screening test, we have developed a portable magnetofuidic instrument and corresponding assay cartridge. The assay cartridges use functionalized magnetic beads to couple nucleic acid extraction directly to a PC-based duplexed nucleic acid amplification test (NAAT). The NAAT targets the oprA gene for NG identification and the gyrA gene for characterization of ciprofloxacin susceptibility. In order to assess assay performance, we analyzed 27 well characterized NG strains and 29 swabs (20 urethral, 9 penile meatal) previously tested by culture.

Results The instrument has a compact footprint (5”x5.3”x3.3”) and runs on a 5V, 2A power supply that can be provided by a small portable battery pack. Detection of NG and genotypic characterization of ciprofloxacin susceptibility was completed in <40 minutes. The cartridge-based assay correctly identified 99% of 27/29 NG isolates as well as 100% (10/10) of the ciprofloxacin-resistant NG strains. All urethral and penile swabs were correctly identified as well (15/15 positive, 14/14 negative).

Conclusion Magnetofuidic assay cartridges allow automation of NAAT-based testing for NG and assessment of antimicrobial susceptibility. The portability, low power consumption, and ease-of-use of our platform has potential for enabling rapid diagnostics at the POC and in low-resource settings to guide targeted use of antimicrobials. Further studies with clinical samples are warranted.

Disclosure No significant relationships.

004.6 PREDICTION OF AVAILABLE DRUG TARGETS OF NEISSERIA GONORRHOEAE BASED ON CODON USAGE PARAMETER

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Background Neisseria gonorrhoeae is a gram negative diplococcus bacterium and the causative agent of the sexually transmitted disease Gonorrhea. It has been recently given the status of ‘superbug’ by World Health Organization because of the increasing antibiotic resistance and unavailability of a viable vaccine candidate targeted against this bacterium. Over the recent years, there have been increasing reports about the use of subtractive genomics to identify potential drug and vaccine targets.

Methods Hence, present study utilizes the knowledge of Codon biasing, a tool to identify the essential genes in N. gonorrhoeae that could be novel therapeutic targets for drug or vaccine development. Through the screening of a total of 2350 genes, we could shortlist 29 ‘essential’ genes from the complete gene set. This selection process was done through calculating CAI scores for individual genes. Through the data-mining of BLAST2GO and InterProScan databases, we could predict the function of these 29 genes.

Results All the selected 29 genes were involved in important cellular functions like DNA replication, energy synthesis and metabolites production. This study also shortlists the essential genes of N. gonorrhoeae that could be used to target Neisseria. We identified a molecule/drug which can be used as a target against essential protein DapD (succinyltransferase).

Conclusion To conclude, through subtractive genomics, we could identify 29 genes that seem to be essential for the survival of the bacteria Neisseria gonorrhoeae. Identification of these genes can be helpful in understanding the pathogenesis of the bacteria as well. Moreover some of these genes are excellent drug targets as these are essential for the growth of bacteria.

Disclosure No significant relationships.